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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/430,029	10/29/1999	TETSUYA YANO	35.C13982	6685

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EXAMINER

SLOBODYANSKY, ELIZABETH

ART UNIT PAPER NUMBER

1652

DATE MAILED: 04/08/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/430,029

Applicant(s)

YANO ET AL.

Examiner

Elizabeth Slobodyansky

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 20 December 2002.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-48 and 55 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 1,2,15,16,19 and 20 is/are allowed.
- 6) ☒ Claim(s) 3-5,9-14,17,18,21-48 and 55 is/are rejected.
- 7) ☒ Claim(s) 6-8 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 26.
- 4) ☐ Interview Summary (PTO-413) Paper No(s) _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

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DETAILED ACTION

The amendment filed December 20, 2002 amending claims 1, 3, 5, 6, 8-10, 13, 17, 19, 21, 27, 33, 34, 48 and 55 has been entered.

Claims 1-48 and 55 are pending.

Claim Objections

Claims 6-8, 11-14 and 55 are objected to because of the following informalities:

In claim 6, line 7, the reference to "of the Sequence Listing" is not necessary.

Claims 7, 8, 11-14 and 55 are objected as dependent from claim 6.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 3-5, 9-14, 17, 18, 21-48 and 55 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a toluene monooxygenase encoded by sequence of SEQ ID NO:1 and a DNA encoding TomK of 234-443 portion of SEQ ID NO: 1, does not reasonably provide enablement for a DNA encoding a toluene monooxygenase and TomK of an unknown amino acid sequence

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encoded by a DNA that hybridizes to said sequences. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir. 1988). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) considered in determining whether undue experimentation is required, are summarized the predictability or unpredictability of the art, and (8) the breadth of the claims.

The instant invention is directed to a gene encoding a toluene monooxygenase having the sequence of SEQ ID NO:1. The above claims are drawn to sequences having structures different from SEQ ID NO: 1 and the 234-443 portion thereof and encoding a polypeptide retaining the requisite function.

The specification does not support the broad scope of the claims which encompass all modifications and fragments of a sequence that comprises SEQ ID NO:1 and its portion and encodes a toluene monooxygenase or TomK activity. This is because the specification does **not** establish: (a) regions of the protein structure which

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may be modified without effecting the specific requisite activity of the polypeptide of the instant invention; (B) the general tolerance of said polypeptide to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid residues with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Despite knowledge in the art to produce mutations in proteins, the specification fails to provide guidance as to where, and what type of (i.e., what amino acid to substitute into, add to or delete from the known sequence), changes in amino acid residues will result in a desired enzymatic activity. The amino acid sequence of a protein determines its structural and functional properties, and predictability of what mutations can be tolerated in a protein's sequence and result in a certain activity is extremely complex, and well outside the realm of routine experimentation, because accurate predictions of a protein's function from mere sequence data are limited.

Furthermore, while recombinant and mutagenesis techniques are known, it is not routine in the art to screen large numbers of mutated proteins or genes where the expectation of obtaining similar activity is unpredictable based on the instant disclosure.

Therefore, one of ordinary skill in the art would require guidance, in order to make a DNA fragment encoding a toluene monooxygenase or TomK having the

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sequence other than SEQ ID NO: 1 and its 234-443 portion, respectively, in a manner reasonably correlated with the scope of the claims. Without such guidance, the experimentation left to those skilled in the art is undue.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.
Claims 3-5, 9-14, 17, 18, 21-48 and 55 are rejected under 35 U.S.C. 112,

second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 3-5, 9-14, 17, 18, 21-48 and 55 recite "stringent hybridization conditions" rendering the metes and bounds of the claims unascertainable. Said conditions are not defined in the specification. Depending on the conditions nucleotide sequences of different structures would hybridize with the given sequence. Without knowing the exact conditions there is no way of knowing nucleotide sequences of what structure (homology) are encompassed by the scope of the claims.

Claims 10, 13 and 55 are confusing as reciting "a polypeptide having a property of enhanced toluene monooxygenase activity" wherein "a polypeptide having a property to enhance toluene monooxygenase activity" appears to be intended.

Claims 17 and 55 are confusing as reciting "an active toluene monooxygenase" and "a toluene monooxygenase" at the same time.

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Claims 22-48 are confusing as drawn to “a method for degrading”, etc. comprising a step of degrading”. Amending the claims to recite “a method for degrading comprising a step of contacting a compound with a transformant”, for example, is suggested.

Response to Arguments

Applicant's arguments filed December 20, 2002 have been fully considered but they are not persuasive.

Applicants argue that “the phrase”under stringent (hybridization) conditions” is a well known and well understood expression to those of ordinary skill in the art. The degree of hybridization or homology between the probe and the nucleic acid is determined by the stringency of the hybridization” (Remarks, page 8). The examiner agrees that the term “hybridization conditions” is well understood by those of ordinary skill in the art. However, “stringent conditions” can mean different conditions and, therefore, homology, in different examples. It means that depending on the exact conditions different molecules will hybridize to the same molecule rendering the metes and bounds of the claim unascertainable. This view is supported by Applicants assertion that “one of ordinary skill in the art can readily adjust conditions for any hybridization so that they are stringent, resulting in a high homology between the probe

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and the nucleic acid" (page 10, emphasis added). The term "high" is a relative term which is indefinite absent a specific definition.

The rejection of claims 22-48 has been reworded and the amendment is suggested.

Of note, if the degree of homology would be defined as at least 90%, for example, both the enablement rejection and 112, 2nd paragraph, rejection will be withdrawn, assuming there is support in the specification. The enablement rejection is made over sequences with a low degree of homology.

Allowable Subject Matter

Claims 1, 2, 15, 16, 19 and 20 are allowed.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not

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mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elizabeth Slobodyansky whose telephone number is (703) 306-3222. The examiner can normally be reached Monday through Friday from 9:30 AM to 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ponnathapura Achutamurthy, can be reached at (703) 308-3804. The FAX phone number for Technology Center 1600 is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Center receptionist whose telephone number is (703) 308-0196.

A handwritten signature in cursive script, reading "E. Slobodyansky". The signature is written in black ink and is positioned above the printed name and title of the examiner.

Elizabeth Slobodyansky, PhD
Primary Examiner

April 3, 2003